prolonged serum levels exceeding 8-10 μg/ml. In cases 1 and 2 the immediate and dramatic changes occurred with levels greater than this. In case 3 lesser changes occurred even though the serum levels were in the "safe" range. The basal turn of the cochlea seems most vulnerable to both immediate and delayed effects, both of which may produce the dissociated pattern of AP response that is well recognised in high-tone sensory deafness of whatever cause.[10]

The speed of onset of the observed effect suggests a direct action at a site in the cochlea, involving a temporary metabolic block—for example, interference with an energy requiring process or blocking of transport of cations across cell membranes. There is experimental and clinical evidence to show that aminoglycosides interfere with calcium metabolism (probably by binding).[11-14] In the lateral line organ of the fish they may block potassium transport.[15] Both these effects are rapid and may be reversed by administering the appropriate cation in solution. Other metabolic effects follow intoxication with aminoglycosides, although their speed of onset is not clearly established. Guinea-pigs treated with tobramycin sustain most outer hair cell damage in areas of the cochlea where there is the least amount and smallest granule size of glycogen—namely, the basal turn. The greatest oxygen consumption of the cochlea occurs in the basal turn, and is decreased by kanamycin.[17] The adenosine triphosphatase hydrolysing system has been shown to be modified within the microstructures of the cochlea after the administration of aminoglycosides.[18] This may have an important effect on the function of the stria vascularis, which uses adenosine triphosphatase to support a sodium-potassium ion pump to maintain endolymphatic homoeostasis. The possibility that interference with protein synthesis caused of our observed changes is ruled out by their speed of onset.

How our findings relate to long-term ototoxicity is not clear. Doses of aminoglycosides are often therapeutically insufficient, however, and monitoring of the serum levels is required not only for ototoxicity but to ensure that adequate doses are administered.

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Falls in the elderly related to postural imbalance

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Summary

Two hundred and forty-three elderly people aged 60 to 96 years were questioned about their falls, and their sway was measured. For comparison sway was also measured in 63 younger subjects. Sway increased with age and was higher in women at all ages. There was no difference in sway between those with no history of falls and those who fell only because of tripping. In both sexes sway was significantly increased in people who fell because of loss of balance and in women whose falls were due to giddiness, drop attacks, turning the head, and rising from bed or a chair. This suggests that there is a physiological decline in postural control with advancing age and also a decline due to disease of the central nervous system.

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Introduction

Although falls in the elderly are common and are associated with appreciable morbidity and mortality, there have been few investigations of their causes. In a random survey of the elderly population Sheldon[1] found that 21% of men and 43% of women were affected. More recently, in a random sample of people over the age of 65 living at home, a history of falls was obtained in 24% of the men and 44% of the women.[2] In both sexes the proportion who fell increased with age.

Describing the pattern of falls in the elderly, Sheldon[3] commented on the many accidental falls that were apparently caused by impaired balance. Although both young and old may trip over a kerb stone or lose their balance while descending stairs, the ability of the young to regain balance rapidly and avoid an actual fall is in strong contrast to what happens to the elderly. Not only are the elderly unable to correct their balance once they have stumbled but also there is probably a change in gait with age, resulting in the feet not being lifted as high as they used to be.[3]

Another feature of falls in the elderly is that the proportion whose falls are due to tripping declines with increasing age. By contrast, drop attacks, giddiness, loss of balance, and postural hypotension are responsible for an increasing proportion of falls with advancing age.

Unsteadiness in standing was described by Romberg as a sign of disordered sensory-motor function, but Sheldon[4] was the first to investigate in detail the changing pattern of unsteadiness with age. He showed that children have more postural sway than adults and that optimum control over these movements is achieved during the late teens and is maintained until about the age of 60, when there is a progressive rise in sway with age. More recently Hasselkus and Shambes[5] have confirmed in a study on women that the elderly sway more than young adults. Sway has also been used to measure the degree of suggestibility in neurotic and normal individuals, although various workers have drawn different conclusions.[6–8] In the present study we have investigated the association between falls and increased sway.

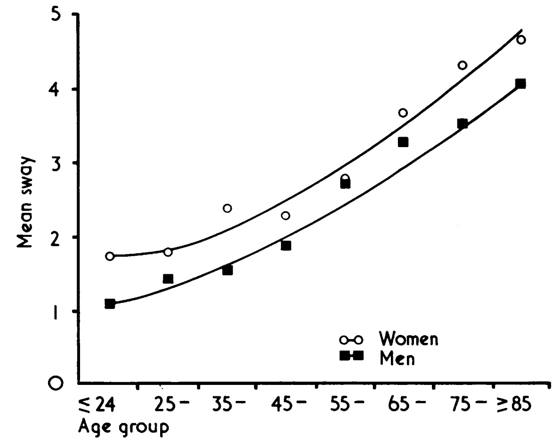

FIG 1—Regression of mean sway on age.

Subjects and methods

A total of 306 people were studied. They consisted of 243 elderly people (105 men and 138 women), whose ages ranged from 60 to 96 years (average 76 years), and, for comparison, 63 younger hospital workers (26 men and 37 women), whose ages ranged from 18 to 59 years. Most of the elderly people were living at home and were either seen at a social centre or were participants in a nutrition survey being conducted in the London Borough of Islington.[2] Those not living at home were 28 army pensioners resident in the Royal Chelsea Hospital. A history was obtained of their falls, current drug treatment, and fractures sustained during the previous 25 years. Sitting and standing blood pressures were measured, and sway was recorded with the ataxiameter described by Wright.[9] This portable apparatus consists of a box placed on the floor from which a vertical mast extends, which is attached by a thread to a belt around the subject's waist. Sway is expressed as total angular movement, summed regardless of sign, in the anterioposterior plane only. Movements are communicated to a double ratchet mechanism in the box, which causes a pointer to rotate continuously over a calibrated dial, each unit of which represents $3\frac{1}{3}°$ of angle of sway. Movements down to one minute of angle are detected.

The subjects, wearing outdoor shoes, stood with their feet comfortably apart and arms by their side. They were asked to look at a distant object and to stand as still as they could while the amount of sway was measured over one minute. The separation of the feet was not standardised and each subject was allowed to assume his position of optimum stability facing the ataxiameter. The test was repeated three times and the mean of the two lowest results was taken as the amount of sway.

Results

Sway increased (non-linearly) with age in both men and women (fig 1), and its distribution in the sample was positively skewed. Logarithmic transformation of sway made the relation with age become linear for both sexes and normalised its distribution. Regression lines for log sway on age, fitted separately for men and women, had slopes that were significantly different from zero ($P<0{\cdot}001$). Comparison of the regression lines for the two sexes indicated no difference between the slopes but a significant difference ($P<0{\cdot}01$) in elevation with the women having more sway than men.

The adequacy of the linear relation between log sway and age was tested by grouping the subjects into eight age groups, fitting regression lines to the means of these groups, and investigating the extent of deviation from linearity. There was no evidence of any departure from a linear relation in either men or women (fig 2).

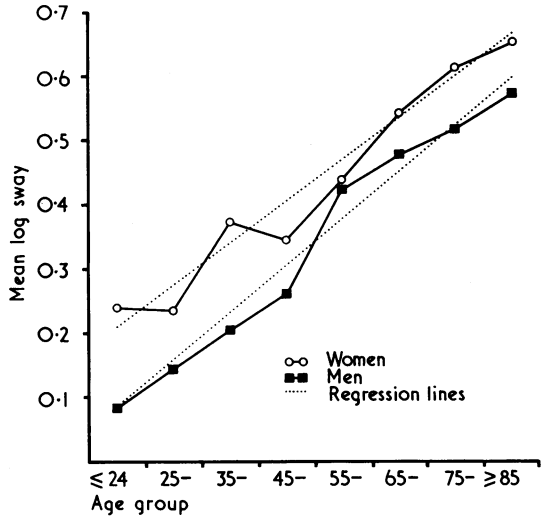

FIG 2—Regression of mean log sway on age.

The 243 subjects aged over 60 were divided into three main groups according to their history of falling. Group 1 consisted of 97 people who had had no falls; group 2 of 69 people who had fallen only because they tripped; and group 3 of 77 people who had had postural falls due to giddiness, drop attacks, loss of balance, turning the head, or rising from a bed or chair. Group 3 also included those who had had falls for unknown reasons or because of poor eyesight, weak legs, or collisions with furniture (miscellaneous cases). A subject's fall was classified as a drop attack if there was a clear history of an unexpected fall without loss of consciousness where no precipitating factor could be identified. Often these subjects reported that they could not stand up immediately afterwards. The causes of falls in table I were those identified by the 146 fallers, some of them having had more than one cause for their falls.

Table II shows the number of subjects and the mean log sway in each group. Comparisons between the means of group 1, 2, and 3 for each age group were made using the least significant difference following an analysis of variance. For both sexes there was no difference between the sway of group 1 and group 2, while the amount of sway in group 3 was significantly higher than that in group 2 for most age groups.

The individual causes of falling in group 3 were examined in more

TABLE I—*Causes of falls as identified by 146 people who had fallen*

	Tripping	Drop attacks	Giddiness	Loss of balance	After rising	Turning head	Miscellaneous	Total
No (%) of subjects	81 (47·1)	21 (12·2)	15 (8·7)	14 (8·2)	11 (6·4)	9 (5·2)	21 (12·2)	172 (100)

TABLE II—*Mean log sway for subjects classified by sex, age, and history of falls. Numbers in each group are given in parentheses*

Age:	60–64	65–74	75–84	≥85
		Men		
1	0·44 (4)	0·45‡ (22)	0·47† (18)	0·57 (11)
2	0·54 (1)	0·44‡ (16)	0·50* (9)	0·42* (3)
3	(0)	0·71 (6)	0·66 (8)	0·66 (7)
		Women		
1	0·45 (6)	0·54 (21)	0·58 (12)	0·62 (3)
2	0·48 (2)	0·47† (18)	0·54* (13)	0·66 (7)
3	0·46 (5)	0·62 (18)	0·66 (28)	0·68 (5)

Significance of difference from mean of corresponding age group for group 3: *$P<0·02$; †$P<0·01$; ‡$P<0·001$.
After logarithmic transformation the data were analysed by analysis of variance: residual variance = 0·020, DF = 220.
Comparisons between pairs of means were made using the least significant difference.

detail by comparing in turn the subjects affected by each cause with those in group 1. Since sway is related to age it is necessary to adjust for age effects when comparing these groups, and this was done by comparing the regressions of log sway on age. Adjusted mean log sway (table III) therefore indicates mean log sway adjusted for age.[10] These adjusted means could be calculated for all groups except men who had fallen after turning their heads, in whom the regression line of log sway on age was not parallel to that from group 1. Sway was increased in all subgroups compared with that in group 1, but this was significant in both sexes only for loss of balance and in women for giddiness, drop attacks, turning the head, and after rising from a bed or a chair.

TABLE III—*Mean log sway adjusted for age of subjects classified by sex and cause of falling. Numbers in each group are given in parentheses*

Group	Adjusted mean log sway	
	Men	Women
No falls (group 1)	0·48 (55)	0·55 (42)
Giddiness	0·56 (5)	0·70§ (10)
Drop attacks	0·52 (1)	0·64† (20)
Loss of balance	0·72‡ (6)	0·67† (8)
Turning head	(4)	0·69† (5)
After rising	0·49 (3)	0·70* (8)
Miscellaneous	0·59 (6)	0·58 (15)

Significance of difference from adjusted mean of group 1: †$P<0·05$; *$P<0·02$; §$P<0·01$; ‡$P<0·001$.

Similar methods were used to examine the relation between sway and postural hypotension, fractures in the previous 25 years, the taking of drugs likely to increase sway, and the frequency of falling in the previous year. The three groups in table II were combined in this analysis.

Postural hypotension—This was defined as a fall in systolic pressure of 20 mm Hg or more between the sitting and standing position. It was present in 15 (14%) men and 22 (16%) women, and was not confined to those who fell after rising. The amount of sway was significantly greater in people with postural hypotension (men $P<0·02$; women $P<0·05$).

Fractures in previous 25 years—Only 8 (8%) men had had a fracture, too few for statistical comparison. Fractures had occurred in 39 (28%) women, half of them affecting the wrist. No difference in the amount of sway was found between those subjects who had sustained fractures and those in the rest of the sample.

Drugs likely to increase sway—Subjects were included in this category if they gave a history of receiving night sedatives, antihypertensives, diuretics, phenothiazines, or benzodiazepines. Twenty-one (20%) men and 46 (33%) women gave such a history but there was no difference in amount of sway for either sex compared with those not receiving drugs.

Falls in previous year—All fallers were divided into three groups according to the number of falls they had had in the previous year: none, one to four, and five or more. Most people in both sexes had fallen between one and four times. No difference was found between the first two groups. Those who had had five or more falls, however, swayed more than those who had had one to four falls (men $P<0·02$; women $P<0·05$) and those who had had none (men $P<0·01$; women $P<0·005$).

Discussion

That elderly people sway more than young ones is not surprising, but it is interesting that this decline in postural control can be shown long before senescence. The finding that at all ages women sway more than men is probably a function of the body weight:muscle mass ratio.[11] Differences in footwear may have accounted for some of the increased sway but this was unlikely since none of the women tested were wearing high-heeled shoes.

No difference in sway was found in either sex between non-fallers and those who had fallen because of a trip. In both these groups there was less sway than in those who had fallen for reasons other than tripping. In women the amount of sway was significantly higher when falls had been due to giddiness, drop attacks, loss of balance, turning the head, or rising from bed or a chair. In men, although all these causes were associated with increased sway, only the results in the loss of balance group were statistically significant.

Hence probably postural control declines physiologically with age, and there is also a decline due to disease, as shown by the increased amount of sway in those who fell for reasons other than tripping. Tripping is an accident that can happen to anyone and is not necessarily associated with disease or increased sway.

Among the causes of falls tripping was found to be the commonest (47%). This compares with Sheldon's[3] total for trips and accidental falls of 45%. Our figure for drop attacks of 12% is lower than Sheldon's 25%, but is close to the 13% found in 536 women over the age of 65 by Exton-Smith.[2] Once again the female preponderance in this disorder is confirmed; 20 women but only one man had suffered from drop attacks.

Exton-Smith[2] showed that the type of fall is related to age in that there is a higher proportion of falls due to causes others than tripping in people aged over 75 years. We have found the same trend, and so did Brocklehurst *et al*[12] in a study of fractures of the femoral neck.

The prevalence of postural hypotension in this sample was 15%. This was lower than the 24% found by Caird *et al*[13] and the 17% found by Johnson *et al*,[14] but in both these studies the postural fall in pressure was recorded between the lying and standing and not the sitting and standing positions.

Sheldon[4] suggested that the change in sway with age was due to a change in the ability to control random movements that originated centrally, and that increased sway in the elderly was due to loss of cells in the brain stem and cerebellum. Hasselkus and Shambes[5] agreed with the theory that ageing causes a decline in the central control of posture. Our finding that sway was increased in those subjects whose falls had been due to giddiness, drop attacks, and turning the head lends support to this theory, although reduced peripheral proprioceptive information in the elderly probably also plays an important part.

Numerous methods have been devised for measuring postural sway,[5, 7, 15–18] but none of them has been brought into regular clinical use since either the equipment is expensive or inconvenient or the results obtained are not immediately available in a simple numerical form. The instrument used in this study has none of these drawbacks and has recently been modified so as to be small and light enough to fit into a pocket.[11] We hope that further studies will be done with the ataxiameter to assess its value in predicting the likelihood of falls.

We thank Major-General R J G Morrison for permission to study patients under his care at the Royal Hospital, Chelsea; Mrs Grace Francis, Miss Christine Thornton, and Mrs Wendy Doyle for help during the project; Miss Ann O'Brien for secretarial work; and Dr B M Wright for helpful suggestions.

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Evaluation of ^{125}I-fibrinogen test for venous thrombosis in patients with hip fractures: comparison between isotope scanning and necropsy findings

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Summary

The results of ^{125}I-fibrinogen leg scanning during life were compared with the findings at a detailed post-mortem dissection of the leg veins in 31 patients with hip fractures who died during the period of isotope scanning or within seven days of the last scan. Thigh scanning on the side of the hip fracture proved valueless, and criteria for the confident isotopic diagnosis of venous thrombosis in the uninjured thigh could not be determined. In the lower leg a difference in uptake of 20% or more that persisted for 24 hours between adjacent positions on one leg or between corresponding positions on the two legs was consistently associated with the presence of venous thrombosis at necropsy.

Introduction

The ^{125}I-fibrinogen test for deep vein thrombosis has been used as an objective diagnostic aid in many clinical trials of potential antithrombotic agents, and the ability of agents to suppress isotopically diagnosed thrombosis has been used as a trial endpoint. During the past decade various criteria have been used[1-6] to diagnose deep vein thrombosis but the most common are those that require a difference in uptake[2] of 15% or 20% between adjacent positions on the same limb or between corresponding positions on the two limbs that persists for 24 hours or more. Close correlations between the results of scanning and venography have been found with both criteria,[4 7 8] but the correlations have related mostly to calf vein thrombosis. Browse *et al*,[5] however, found a good correlation between the results of scanning and venography in the middle and distal thirds of the thigh as well as in the calf in established venous thrombosis.

Assessments of the isotope method, using venography as a yardstick, have mainly been carried out in general surgical patients and there has been only a limited evaluation of the ^{125}I-fibrinogen test in patients subjected to leg surgery in whom high counts will occur near the operation site even in the absence of venous thrombosis. The two studies in which the ^{125}I-fibrinogen test and venography have been compared in patients with hip fractures or hip replacements have shown that either the isotope test overdiagnoses or venography underdiagnoses venous thrombosis[9 10] in these patients. Our study was undertaken to validate the results of scanning against the necropsy findings in patients with hip fractures to determine the limitations of the ^{125}I-fibrinogen test in such patients and to calibrate the test, if possible, for use in patients with hip fractures.

Methods

During a series of clinical trials in which the ^{125}I-fibrinogen test was used in over 300 patients with hip fractures[11] 31 patients died during the scanning period or within seven days of the last scan. Detailed dissection of the leg veins was performed in those patients so that the results of isotope scanning during life could be compared with the necropsy findings.

^{125}I-fibrinogen scanning technique—Supplies of ^{125}I-fibrinogen were obtained from the Radiochemical Centre, Amersham. Each patient received an intravenous injection of 100 μCi of the labelled fibrinogen after the thyroid gland uptake had been suppressed by an intravenous injection of sodium iodide (100 mg). Oral sodium iodide (100 mg) was then administered twice daily for 28 days thereafter. The isotope was injected as soon as possible after admission, and the injection was never delayed more than 48 hours after the patient's admission to hospital. Scanning with a Nuclear Enterprises Scaler/Ratemeter (fitted with a GP7 scintillation probe) was performed daily thereafter, omitting weekends, for 10 days or until the patient died. At the initial examination the maximum count over the heart was obtained and this position was marked so that subsequent praecordial counts could be obtained from the same position. Counting positions on the legs were also marked; these positions were at 5-cm intervals from the mid-inguinal point down the medial aspect of the thigh over the course of the femoral vein and down the posterior aspect of the calf from the popliteal fossa to the ankle.

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